Complete Summary

GUIDELINE TITLE

Selective estrogen receptor modulators.

BIBLIOGRAPHIC SOURCE(S)

American College of Obstetricians and Gynecologists (ACOG). Selective estrogen receptor modulators. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2002 Oct. 10 p. (ACOG practice bulletin; no. 39). [67 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Breast cancer
- Osteoporosis
- Menopausal symptoms

GUIDELINE CATEGORY

Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Obstetrics and Gynecology
Oncology
Preventive Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To review the use of selective estrogen receptor modulators (SERMs) for breast cancer risk reduction and skeletal protection as approved by the U.S. Food and Drug Administration (FDA)
- To aid practitioners in making decisions about appropriate obstetric and gynecologic care

TARGET POPULATION

Women with breast cancer or osteoporosis or at high risk of breast cancer or osteoporosis

INTERVENTIONS AND PRACTICES CONSIDERED

Breast Cancer Prevention and Treatment

1. Breast cancer risk assessment
2. Tamoxifen therapy
3. Routine gynecologic care
4. Monitoring patients for any abnormal uterine or vaginal bleeding
5. Co-administration of local vaginal estrogen therapy for the relief of vaginal dryness

Osteoporosis Prevention and Treatment

1. Raloxifene therapy
2. Combined use of raloxifene and alendronate
3. Routine gynecologic care
4. Monitoring patients for any abnormal uterine or vaginal bleeding
5. Co-administration of local vaginal estrogen therapy for the relief of vaginal dryness

MAJOR OUTCOMES CONSIDERED

- Risk of estrogen-receptor breast cancer
- Bone fracture risk and fracture rate
- Risk of uterine cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' (ACOG's) own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and November 2001. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document.

Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force.

I Evidence obtained from at least one properly designed randomized controlled trial

II-1 Evidence obtained from well-designed controlled trials without randomization

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Analysis of available evidence was given priority in formulating recommendations. When reliable research was not available, expert opinions from obstetrician-gynecologists were used. See also the "Rating Scheme for the Strength of Recommendations" field regarding Grade C recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A - Recommendations are based on good and consistent scientific evidence.

Level B - Recommendations are based on limited or inconsistent scientific evidence.

Level C - Recommendations are based primarily on consensus and expert opinion.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practice Bulletins are validated by two internal clinical review panels composed of practicing obstetrician-gynecologists generalists and sub-specialists. The final guidelines are also reviewed and approved by the American College of Obstetricians and Gynecologists (ACOG) Executive Board.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of evidence (I-III) and levels of recommendations (A-C) are defined at the end of the "Major Recommendations."

The following recommendations are based on good and consistent scientific evidence (Level A):

- Consideration should be given to tamoxifen therapy for women at high risk for developing breast cancer.
- Raloxifene is appropriate therapy for women who are candidates for chemoprevention of osteoporosis.
- Raloxifene is appropriate therapy for women with established osteoporosis to prevent osteoporotic fractures.
- Neither raloxifene nor tamoxifen should be used in women with a history of venous thromboembolic events, including pulmonary emboli, deep vein thrombosis, or retinal vein thrombosis.
- Any abnormal uterine bleeding should be investigated in women taking tamoxifen or raloxifene.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- Because there are no data on the use of raloxifene in women who have completed a 5-year course of tamoxifen therapy, such women should have an individual assessment of their risk of osteoporosis, and decisions about prevention or treatment should be made accordingly.
- The use of tamoxifen for chemoprevention should be limited to 5 years.
- Co-administration of local vaginal estrogen therapy may be used for the relief of vaginal dryness in patients receiving raloxifene or tamoxifen therapy.
- Individualized risk assessment should be performed to determine whether a patient is a candidate for breast cancer risk reduction by chemoprevention, unless she has ductal carcinoma in situ or lobular carcinoma in situ, in which case the benefit of chemoprevention already has been documented.

Definitions:

Grades of Evidence

I Evidence obtained from at least one properly designed randomized controlled trial

II-1 Evidence obtained from well-designed controlled trials without randomization

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Levels of Recommendations

Level A - Recommendations are based on good and consistent scientific evidence.

Level B - Recommendations are based on limited or inconsistent scientific evidence.

Level C - Recommendations are based primarily on consensus and expert opinion.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Benefits of Specific Medication

- Raloxifene. In clinical trials for the treatment of osteoporosis, raloxifene was associated with a significant reduction in new-onset cases of breast cancer when measured as a secondary endpoint in low-risk women. A significant risk reduction for vertebral fracture and pelvic floor surgery among women treated for 3 years was also demonstrated.
- Tamoxifen. Tamoxifen is associated with reduced risk of both invasive and noninvasive breast cancer.
- Both tamoxifen and raloxifene have been shown to have favorable cardiovascular effects.

POTENTIAL HARMS

Side Effects of Selective Estrogen Receptor Modulators (SERMs)

- Tamoxifen. Tamoxifen has been associated with endometrial thickening, endometrial polyps, endometrial cystic atrophy, endometrial hyperplasia, a twofold to fourfold increased risk for endometrial cancer, and a small but increased risk of uterine sarcoma. In addition, vaginal bleeding, vaginal discharge, venous thromboembolism, and hot flashes have also been reported in patients treated with tamoxifen.
- Raloxifene. Raloxifene is associated with hot flashes and an increased risk for venous thromboembolism.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Raloxifene. Raloxifene is contraindicated in pregnant women or those who may become pregnant.
- Raloxifene and tamoxifen. Neither raloxifene nor tamoxifen should be used in women with a history of venous thromboembolic events, including pulmonary emboli, deep vein thrombosis, or retinal vein thrombosis.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 (revised 2002 Oct)

GUIDELINE DEVELOPER(S)

American College of Obstetricians and Gynecologists - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Obstetricians and Gynecologists (ACOG)

GUIDELINE COMMITTEE

American College of Obstetricians and Gynecologists (ACOG) Committee on Practice Bulletins-Gynecology

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American College of Obstetricians and Gynecologists (ACOG). Selective estrogen receptor modulators. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 1999 Oct.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 4500, Kearneysville, WV 25430-4500; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on February 4, 2004. The information was verified by the guideline developer on July 26, 2004.

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